



## Complete Summary

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### GUIDELINE TITLE

Hormone replacement therapy.

### BIBLIOGRAPHIC SOURCE(S)

Singapore Ministry of Health, Singapore Academy of Medicine, Chapter of Obstetricians and Gynaecologists. Hormone replacement therapy. Singapore: Singapore Ministry of Health; 2004 Apr. 30 p. [51 references]

## COMPLETE SUMMARY CONTENT

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INSTITUTE OF MEDICINE (IOM) NATIONAL HEALTHCARE QUALITY REPORT

### CATEGORIES

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## SCOPE

### DISEASE/CONDITION(S)

- Symptoms of menopause, including vasomotor symptoms, vaginal dryness, and urinary symptoms
- Premature menopause

Note: Conditions for which hormone replacement therapy is NOT indicated are also discussed. These include osteoporosis, heart disease, dementia, and colorectal cancer.

### GUIDELINE CATEGORY

Evaluation  
Management  
Prevention  
Treatment

### CLINICAL SPECIALTY

Family Practice  
Geriatrics  
Obstetrics and Gynecology

## INTENDED USERS

Advanced Practice Nurses  
Allied Health Personnel  
Pharmacists  
Physicians

## GUIDELINE OBJECTIVE(S)

- To address the following issues:
  - Indications for the use of hormone replacement therapy in the healthy postmenopausal woman
  - Safety issues in the use of hormone replacement therapy
  - Principles of treatment, dosing, and optimal duration of therapy
  - Treatment of premature menopause
  - Answers to frequently asked questions about hormone replacement therapy
- To discuss the implications of the Women's Health Initiative study (WHI), a large randomized controlled trial, on the role of hormone replacement therapy in stroke, cardiovascular disease, and various cancers

## TARGET POPULATION

Women in Singapore with premature menopause or symptoms of menopause

## INTERVENTIONS AND PRACTICES CONSIDERED

Hormone replacement therapy, including indications for use, dosage, duration, and route of medications:

1. Estrogens, oral: conjugated equine estrogen (Premarin); estradiol (Estrafem); estradiol valerate (Proginova)
2. Estrogens, transdermal: estradiol patch (Estraderm); estrogen; estradiol hemihydrate (Estrava gel)
3. Progestogens: medroxyprogesterone acetate (Provera); dydrogesterone (Duphaston); norethisterone (Micronor); intrauterine L-norgestrel system (Mirena); micronised progesterone (Utrogestan)
4. Cyclical combined therapies: estradiol valerate and norgestrel (Progyluton); estradiol valerate and cyproterone acetate (Climens); conjugated equine estrogen and norgestrel (Prempak-C); conjugated equine estrogen and medroxyprogesterone acetate (Premelle cycle 5); estradiol and dydrogesterone (Femoston); estradiol and norethisterone acetate (Trisequens)
5. Continuous combined therapies: conjugated equine estrogen and medroxyprogesterone acetate (Premelle 5 or Premelle 2.5); estradiol and norethisterone acetate (Kliogest or Activelle).

6. Local therapy: estradiol pessary (Vagifem); conjugated equine estrogen cream (Premarin cream); colpotrophine 1% cream; colpotrophine pessary 10%; estradiol ring (Estring)

#### MAJOR OUTCOMES CONSIDERED

- Relief of menopausal symptoms
- Long-term risks of prolonged estrogen deficiency
- Adverse effects of hormone replacement therapy, both short-term and long-term

### METHODOLOGY

#### METHODS USED TO COLLECT/SELECT EVIDENCE

Searches of Electronic Databases

#### DESCRIPTION OF METHODS USED TO COLLECT/SELECT THE EVIDENCE

Not stated

#### NUMBER OF SOURCE DOCUMENTS

Not stated

#### METHODS USED TO ASSESS THE QUALITY AND STRENGTH OF THE EVIDENCE

Weighting According to a Rating Scheme (Scheme Given)

#### RATING SCHEME FOR THE STRENGTH OF THE EVIDENCE

Levels of Evidence

Level Ia: Evidence obtained from meta-analysis of randomised controlled trials

Level Ib: Evidence obtained from at least one randomised controlled trial

Level IIa: Evidence obtained from at least one well-designed controlled study without randomisation

Level IIb: Evidence obtained from at least one other type of well-designed quasi-experimental study

Level III: Evidence obtained from well-designed nonexperimental descriptive studies, such as comparative studies, correlation studies, and case studies

Level IV: Evidence obtained from expert committee reports or opinions and/or clinical experiences of respected authorities

## METHODS USED TO ANALYZE THE EVIDENCE

Review of Published Meta-Analyses  
Systematic Review

## DESCRIPTION OF THE METHODS USED TO ANALYZE THE EVIDENCE

Not stated

## METHODS USED TO FORMULATE THE RECOMMENDATIONS

Expert Consensus

## DESCRIPTION OF METHODS USED TO FORMULATE THE RECOMMENDATIONS

These guidelines were developed by a workgroup made up of specialists in the field of obstetrics and gynaecology with a special interest in hormone replacement therapy and care of menopausal woman, as well as a family practitioner. An exhaustive search into the medical literature as well as guidelines from various colleges around the world formed the basis of these guidelines and recommendations.

## RATING SCHEME FOR THE STRENGTH OF THE RECOMMENDATIONS

### Grades of Recommendations

Grade A (evidence levels Ia, Ib): Requires at least one randomised controlled trial as part of the body of literature of overall good quality and consistency addressing the specific recommendation.

Grade B (evidence levels IIa, IIb, III): Requires availability of well conducted clinical studies but no randomised clinical trials on the topic of recommendation.

Grade C (evidence level IV): Requires evidence obtained from expert committee reports or opinions and/or clinical experiences of respected authorities. Indicates absence of directly applicable clinical studies of good quality.

GPP (good practice points): Recommended best practice based on the clinical experience of the guideline development group.

## COST ANALYSIS

A formal cost analysis was not performed and published cost analyses were not reviewed.

## METHOD OF GUIDELINE VALIDATION

Not stated

## DESCRIPTION OF METHOD OF GUIDELINE VALIDATION

Not applicable

## RECOMMENDATIONS

### MAJOR RECOMMENDATIONS

The recommendations that follow are those from the guideline's executive summary; detailed recommendations can be found in the original guideline document. Each recommendation is rated based on the level of the evidence and the grades of recommendation. Definitions of the grades of the recommendations (A, B, C, Good Practice Points [GPP]) and level of the evidence (Level I–Level IV) are presented at the end of the Major Recommendations field.

A – Hormone replacement therapy (HRT) is recommended for the short-term control of vasomotor symptoms, vaginal dryness, and urinary symptoms in menopause. (Grade A, Level Ib)

C - Combination HRT should not be used to reduce the risk of osteoporosis and subsequent fractures if it is the only indication for starting hormone replacement therapy. Alternatives such as bisphosphonates (Black et al., 1996) and raloxifene (Ettinger et al., 1999) should instead be considered. (Grade C, Level IV)

A - HRT should not be used for primary or secondary prevention of heart disease. (Grade A, Level Ib)

C - Prevention of colorectal cancer should not be the reason for long-term hormone replacement therapy. (Grade C, Level IV)

A - HRT is not recommended for the prevention of Alzheimer's disease or dementia. (Grade A, Level Ib)

A - The use of unopposed HRT in a woman with an intact uterus has been shown to increase the risk of endometrial cancer by several fold (Chlebowski et al., 2003; Shields et al., 1999). Therefore combined hormone replacement therapy should be used in patients with intact uteri. (Grade A, Level Ia)

C - HRT is the cornerstone in the management of patients with premature menopause. It is effective in the relief of menopausal symptoms and protects against the long-term risks associated with prolonged estrogen deficiency ("Risks and benefits of estrogen," 2002; Davis, 1996; Willhite & O'Connell, 2001; Cardozo et al, 1998). (Grade C, Level IV)

### Grades of Recommendations

Grade A (evidence levels Ia, Ib): Requires at least one randomised controlled trial as part of the body of literature of overall good quality and consistency addressing the specific recommendation.

Grade B (evidence levels IIa, IIb, III): Requires availability of well conducted clinical studies but no randomised clinical trials on the topic of recommendation.

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GPP (good practice points): Recommended best practice based on the clinical experience of the guideline development group.

#### Levels of Evidence

Level Ia: Evidence obtained from meta-analysis of randomised controlled trials

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Level IIa: Evidence obtained from at least one well-designed controlled study without randomisation

Level IIb: Evidence obtained from at least one other type of well-designed quasi-experimental study

Level III: Evidence obtained from well-designed nonexperimental descriptive studies, such as comparative studies, correlation studies and case studies

Level IV: Evidence obtained from expert committee reports or opinions and/or clinical experiences of respected authorities

#### CLINICAL ALGORITHM(S)

None provided

### EVIDENCE SUPPORTING THE RECOMMENDATIONS

#### REFERENCES SUPPORTING THE RECOMMENDATIONS

[References open in a new window](#)

#### TYPE OF EVIDENCE SUPPORTING THE RECOMMENDATIONS

The type of supporting evidence is identified and graded for each recommendation (see "Major Recommendations")

### BENEFITS/HARMS OF IMPLEMENTING THE GUIDELINE RECOMMENDATIONS

#### POTENTIAL BENEFITS

- Short-term hormone replacement therapy (HRT) helps control menopausal vasomotor symptoms, urinary symptoms, and symptoms of vaginal dryness.

- HRT is the cornerstone in the management of patients with premature menopause. It is effective in the relief of significant menopausal symptoms and protects against the long-term risks associated with prolonged estrogen deficiency.
- In the Women's Health Initiative (WHI) study, a large randomized controlled trial, combination HRT was associated with reduced risk of endometrial cancer, hip fractures, and colorectal cancers. Estrogen alone appears to marginally decrease risk of hip fracture in postmenopausal women with hysterectomies.

## POTENTIAL HARMS

- Combination hormone replacement therapy (HRT) is associated with significant risk of deep vein thrombosis and pulmonary embolism.
- Combination HRT is associated with a small increase of ischaemic stroke in healthy postmenopausal women. Results with estrogen alone replacement indicated that the increased risk of stroke is similar to that found in the trial of estrogen plus progestin when it was stopped after 5.2 years of follow up.
- Combination HRT, and unopposed estrogen replacement therapy are associated with a small but significant risk of breast cancer. Estrogen only therapy did not show an increased risk in hysterectomized women.
- Combination HRT is associated with a doubled rate of dementia including Alzheimer's disease.
- There is evidence that mammographic changes associated with hormone usage may hinder and delay the diagnosis of breast cancer.
- Other HRT side effects are breast tenderness, irregular vaginal bleeding, and headaches.

## CONTRAINDICATIONS

### CONTRAINDICATIONS

The use of unopposed hormone replacement therapy (HRT) in a woman with an intact uterus has been shown to increase the risk of endometrial cancer by several fold. Therefore combined HRT should be used in patients with intact uteri.

## QUALIFYING STATEMENTS

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- These guidelines are not intended to serve as a standard of medical care. Standards of medical care are determined on the basis of all clinical data available for an individual case and are subject to change as scientific knowledge advances and patterns of care evolve.
- The contents of this publication are guidelines to clinical practice, based on the best available evidence at the time of development. Adherence to these guidelines may not ensure a successful outcome in every case, nor should they be construed as including all proper methods of care or excluding other acceptable methods of care. Each physician is ultimately responsible for the management of his/her unique patient in the light of the clinical data presented by the patient and the diagnostic and treatment options available.

## IMPLEMENTATION OF THE GUIDELINE

### DESCRIPTION OF IMPLEMENTATION STRATEGY

The guidelines propose the following audit parameter:

Percentage of women with intact uteri on hormone replacement therapy receiving estrogen-only therapy. (The use of unopposed hormone replacement therapy in a woman with an intact uterus has been shown to increase the risk of endometrial cancer by several fold. Therefore combined hormone replacement therapy should be used in patients with intact uteri.)

## INSTITUTE OF MEDICINE (IOM) NATIONAL HEALTHCARE QUALITY REPORT CATEGORIES

### IOM CARE NEED

Getting Better  
Staying Healthy

### IOM DOMAIN

Effectiveness

## IDENTIFYING INFORMATION AND AVAILABILITY

### BIBLIOGRAPHIC SOURCE(S)

Singapore Ministry of Health, Singapore Academy of Medicine, Chapter of Obstetricians and Gynaecologists. Hormone replacement therapy. Singapore: Singapore Ministry of Health; 2004 Apr. 30 p. [51 references]

### ADAPTATION

Not applicable: The guideline was not adapted from another source.

### DATE RELEASED

2004 Apr

### GUIDELINE DEVELOPER(S)

Chapter of Obstetricians and Gynaecologists, Academy of Medicine (Singapore) - Medical Specialty Society  
Singapore Ministry of Health - National Government Agency [Non-U.S.]

### SOURCE(S) OF FUNDING



Singapore Ministry of Health (MOH)

## GUIDELINE COMMITTEE

Workgroup on Hormone Replacement Therapy

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## FINANCIAL DISCLOSURES/CONFLICTS OF INTEREST

Not stated

## GUIDELINE STATUS

This is the current release of the guideline.

## GUIDELINE AVAILABILITY

Electronic copies: Available in Portable Document Format (PDF) from the [Singapore Ministry of Health Web site](#).

Print copies: Available from the Singapore Ministry of Health, College of Medicine Building, Mezzanine Floor 16 College Rd, Singapore 169854.

## AVAILABILITY OF COMPANION DOCUMENTS

None available

## PATIENT RESOURCES

None available

## NGC STATUS

This NGC summary was completed by ECRI on July 28, 2004.

## COPYRIGHT STATEMENT

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